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	Examiner Name	Liu, Sue Xu
	Title: "Methods For Depositing Small Volumes Of Protein Fluids Onto The Surface Of A Substrate"	

Sir:

This Reply Brief is in response to the Examiner's Answer dated May 13, 2008.

The Commissioner is hereby authorized to charge deposit account number 50-1078, reference no. 10991398-1 to cover any required fees.

REPLY BRIEF

In this Reply Brief, the Appellants address several issues raised in the Examiner's Answer. The Appellants note that all arguments presented in the prior Appeal Brief still apply with equal force, but are not reiterated here solely in the interest of brevity and for the convenience of the Board.

In this Reply Brief, the issues are first summarized, and the Examiner's assertions are then addressed in eight sections, providing a response to the arguments in the Examiner's Answer of May 13, 2008.

Claims 1, 2, 4, 6-10, 12, 13, 15-18, 20, 21, and 35-38 are not anticipated under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) by Caren et al. (U.S. Patent 6,221,653).

As discussed in the Appeal Brief, an element of all three independent claims is depositing a quantity of fluid containing a protein reagent of interest (Claim 1), a protein reagent binding pair member (Claim 12), or an enzyme reagent (Claim 17) onto a surface of a substrate in a manner that retains the deposited reagent's functionality.

In maintaining the rejection of the claims over Caren '653, the Office continues to assert that "reagent", "which, given the broadest and reasonable interpretation, means a fluid containing a protein." And further, "[a]s long as a fluid that is being deposited contains proteins, the fluid reads on the claimed "fluid containing a protein reagent". (Examiner's Answer, p. 15)

In other words, the Office is basing the rejection on a reading of the claims that interprets "reagent" as any protein. It appears to the Appellants that the Office is maintaining that "reagent" has no meaning beyond that of "protein".

As discussed in the Appeal Brief, a reagent is defined as follows: "a substance used in a chemical reaction to detect, measure, examine, or produce other substances." (American Heritage Dictionary). In other words, a reagent as in the current claims is a substance, for example, used to detect the presence of an analyte.

The Appellants maintain that while *In re Morris* cites giving the "broadest reasonable meaning of the words", *In re Morris* also instructs to take "into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification".

The Appellants respectfully submit that the current claims and specification are clear as to the definition and meaning of depositing a reagent onto the surface of a substrate. The Appellants maintain that a reagent as defined in the specification and as is known in the art is distinct from an analyte in a sample. The deposited reagent of the current claims is used to produce arrays for detecting analyte in a sample:

> "The subject arrays produced in accordance with the invention find use in a variety microarray applications, including analyte detection applications in which the presence of a particular analyte in a given sample may be detected. Protocols for carrying out such assays are well known to those of skill in the art and need not be described in detail herein. Briefly, a sample comprising the analyte of interest is contacted with an array produced according to the subject methods under conditions sufficient for the analyte to bind to its respective binding pair member that is present on the array. Thus, if the analyte of interest is present in the sample, it binds to the array at the site of its complementary binding member and a complex is formed on the array surface. The presence of this binding complex on the array surface is then detected, e.g. through use of a signal production system, e.g. an isotopic or fluorescent label present on the analyte, etc. The presence of the analyte in the sample is then deduced from the detection of binding complexes on the substrate surface. "(p. 13, lines 11-23)

In other words, an array produced in accordance with the invention is used to "measure" or "examine" a sample for the presence of an analyte. The Office, however, continues to maintain that the proteins in the sample fluid of Caren '653 are used to "measure" or "examine" the binding agent on the array substrate (Examiner's Answer, p. 16). The Office appears to be suggesting that one of skill in the art would deposit a sample, such as a blood sample, on an array to "detect", "measure" or "examine" the array. This is in fact the opposite of protocols for using assays that are well known to those of skill in the art. The Appellants respectfully suggest that if one wished to "measure", or "examine" an array that had been produced, one of skill in the art would not deposit a physiological fluid of unknown composition.

Additionally, the Office has not pointed to where Caren '653 discloses "measuring" or "examining" the binding array. The Appellants maintain that nowhere in

Caren '653 is disclosed a method of "measuring" the binding array, because Caren '653 is directed to deposition of a sample that may or may not contain an analyte of interest.

Furthermore, the Appellants argue that the meaning of "reagent" is clear to those of ordinary skill in the art, and that information which is well known in the art need not be described in detail in the specification (*In re Buchner* 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc. 231 USPQ 81, 94 (Fed. Cir. 1986); and Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co. 221 USPQ 481, 489 (Fed. Cir. 1984)).

The Office continues to assert that the portions of the specification cited in the Appeal Brief do not provide support for a specific definition of protein reagent. The Office states "[t]he second paragraph provides a general recitation of making various arrays, and the 3rd paragraph is reciting a DNA microarray (not protein arrays or protein reagents)." (Examiner's Answer, p. 15)

The Appellants respectfully disagree, and maintain that in addition to the fact that the meaning of "reagent" is clear to those of ordinary skill in the art, the instant specification is clear as to the use of the term "protein reagent" in the current claims. The citations in question are reproduced again below for convenience, with emphasis added for clarity:

> "Accordingly, there is continued interest in the development of new protocols for use in the deposition of fluids containing proteins onto a substrate surface. Of particular interest would be the development of a protocol that ... allows the flexibility to change the protein solution deposited and deliver multiple reagents simultaneously. "(p. 2, lines 8-14)

And further:

> "The subject methods of depositing a volume of fluid sample onto the surface of a substrate find use in a variety of different applications, and are particularly suited for use in methods where reproducible placement of small volumes of a reagent onto the surface of a solid support are desired. As such, the subject methods find use in the preparation and manufacture of biosensors, microarrays, e.g., proteomic arrays, microfluidic devices, and the like. (p. 12, lines 28-p. 13, line 1)

And in Example IV:

> "... The slide is then scanned for covalently linked Cy5-dCMP to the DNA attached to the

surface, indicating that the DNA polymerase synthesized DNA. The results show that multiple reagents may be deposited onto the surface using the subject methods. (p. 17, lines 6-9)

The Appellants respectfully submit that the specification is clear as to the meaning of a "quantity of fluid containing a protein reagent of interest" as in Claim 1, or the "quantity of fluid containing a protein reagent binding pair member" of Claim 12, or the "quantity of fluid containing an enzyme reagent" of Claim 17 is clear. As discussed above, the Appellants maintain that the "reagent" of the current claims is not the same as any fluid containing proteins, as the Office suggests.

In sum, a protein reagent as claimed is distinct from a protein analyte, as the reagent that is deposited in the claims is a protein and participates is a substance used in a process to detect an analyte, but is not the analyte itself.

Accordingly, the Appellants maintain that the meaning of "reagent" as in the current claims is clear from the claims, the specification, as well as to those of ordinary skill in the art. Therefore, because Caren '653 does not teach the method of depositing a quantity of fluid containing a protein reagent, or protein reagent binding pair member or enzyme reagent onto a surface of a substrate, Caren '653 does not anticipate the rejected claims.

In view of the discussion above, the Appellants submit that Caren '653 fails to anticipate Claims 1, 2, 4, 6-10, 12, 13, 15-18, 20, 21, and 35-38, and respectfully request reversal of the rejection.

II. Claims 1, 2, 4, 6-10, 12, 13, 15-18, 20, 21, and 35-38 are not anticipated under 35 U.S.C. § 102(e) by Caren et al. (U.S. Patent 6,797,469).

As discussed in the Appeal Brief, an element of all three independent claims is depositing a quantity of fluid containing a protein reagent of interest (Claim 1), a protein reagent binding pair member (Claim 12), or an enzyme reagent (Claim 17) onto a surface of a substrate in a manner that retains the deposited reagent's functionality.

In maintaining the rejection of the claims over Caren '469, the Office continues to assert that "the '469 patent teaches the deposited "quantity of fluid" comprises polypeptides (i.e. protein or a member of a specific binding pair) and enzymes (e.g. Claim 19; col. 4, lines 25+) which reads on the protein reagent of clms 1, 7, 8, 12, 17, 36-38." (Examiner's Answer, p. 18).

However, as discussed above, the Appellants respectfully disagree. Caren '469 is directed to deposition of sample, not reagent, on an array. The cited portions of Caren '469 are directed to screening a fluid sample for the presence of an analyte in a sample; specifically a nucleic acid. As described in the specification, "[T]he fluid sample that is deposited on the array according to the subject invention is a fluid sample that is suspected of containing an analyte of interest. In other words, the fluid sample may or may not actually contain the analyte of interest" (col. 4, lines 14-18). It is therefore not a protein reagent as claimed.

The Office is basing the rejection on a reading of the claims that interprets "reagent" as any protein. A reagent is defined as a substance used in a chemical reaction to detect, measure, examine, or produce other substances. In other words, a reagent as in the current claims is a substance, for example, used to detect the presence of a nucleic acid. This is in contrast to an analyte, (e.g. a nucleic acid) which is "a substance or chemical constituent that is undergoing analysis" (American Heritage Stedmans Medical Dictionary), e.g. a substance that is detected. The Examiner has not pointed to where '469 discloses deposition of a reagent. Nowhere does Caren '469 disclose deposition of a protein reagent onto a substrate in a manner that maintains the reagent's functionality.

The Office maintains that the proteins in the sample fluid of Caren '469 are "used to bind to "measure" or "examine" the binding agent on the array substrate" (Examiner's Answer, p. 18-19), however the Office has not pointed to where Caren '469 discloses "measuring" or "examining" the binding array. The Appellants refer to the discussion above, and additionally maintain that nowhere in Caren '469 is disclosed a method of "measuring" the binding array, because Caren '469 is directed to deposition of a sample

that may or may not contain an analyte of interest.

Accordingly, the Appellants maintain that the meaning of "reagent" as in the current claims is clear from the claims, the specification, as well as to those of ordinary skill in the art and excludes an analyte. Therefore, because Caren '469 does not teach the method of depositing a quantity of fluid containing a protein reagent, or protein reagent binding pair of interest onto a surface of a substrate, Caren '469 does not anticipate the rejected claims.

In view of the discussion above, the Appellants submit that Caren '469 fails to anticipate Claims 1, 2, 4, 6-10, 12, 13, 15-18, 20, 21, and 35-38, and respectfully request reversal of the rejection.

III. Claims 1, 2, 4-10, 12-28, and 35-39 are not anticipated under 35 U.S.C. § 102(b) by, or alternatively, are not obvious under 35 U.S.C. § 103(a) over Deeg et al. (U.S. Patent 5,338,688).

An element of the claims is front loading a fluid into an inkjet head by contacting an orifice with the fluid in a manner so that the fluid flows through the orifice and into a firing chamber.

In making the rejection, the Examiner again alleges that "[a]lthough the '688 patent does not explicitly teach the step of "front loading said quantity of fluid into a thermal inkjet head....", the claimed thermal inkjet head inherently performs "front loading" process. " (Examiner's Answer, p. 20) The Office also alleges that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference". (Examiner's Answer, p. 21)

However, the Appellants argue that the Examiner has not shown that the inkjet head orifice of Deeg, in its normal and usual operation, necessarily performs the "inherent function of capillary suction" when in contact with a fluid. The inkjet orifice of

Deeg does not necessarily perform the "inherent function of capillary suction" because the "normal and usual operation" of Deeg is to load analytical liquid into "disposable jet units" (i.e., cartridges) "which contain the analytical liquid (especially reagents or calibrating liquids) in prepacked form" which are then associated with the inkjet head (column 2, lines 22 to 25).

As discussed in the Appeal Brief, the Appellants maintain that in order to anticipate, the prior art reference "must describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it." In re Spada, 911 F.2d 705, 708, 15 U.S.P.Q.2d (BNA) 1655, 1657 (Fed. Cir. 1990).

Establishing inherency requires that the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. . . . Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268-69, 20 U.S.P.Q.2d (BNA) 1746, 1749 (Fed. Cir. 1991) (quoting In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. (BNA) 323, 326 (C.C.P.A. 1981). In relying on this theory of inherency, one must "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inf. 1990).

The Appellants contend that Deeg does not disclose the front loading of a fluid into an inkjet head. The methods disclosed by Deeg describe a traditional use of inkjet heads, where the fluid comes from a reservoir into the firing chamber, and therefore fluid does not go from the orifice into the firing chamber. The Appellants maintain that nowhere does Deeg teach front loading a fluid into an inkjet head by contacting an orifice with the fluid in a manner so that the fluid flows through the orifice and into a firing chamber.

The Office also alleges that "if fluids are present in the inkjet heads, the fluids are being "front loaded" (due to capillary actions) as the term is broadly defined in the specification." (Examiner's Reply, p. 23)

It is unclear to the Appellants what the Examiner means by this statement. The claimed invention is directed to a method of "contacting said orifice with said fluid in a manner so that said fluid flows through said orifice into said firing chamber" (emphasis added). In other words, in the claimed method, fluid which is to be loaded into the thermal inkjet head is initially outside of the orifice, then flows through the orifice, until it reaches the firing chamber. The Appellants point out that the claimed method of loading fluid into the inkjet head is in the opposite direction of the fluid loading as disclosed in Deeg. It appears that the Examiner is equating any fluids that are present in the inkjet heads as being "front loaded". The Examiner, however, has not pointed to any evidence or reference showing how the mere fact that fluid is present in the ink jet head indicates that the fluid flowed through the orifice in the manner of front loading that is disclosed in the Appellants' claimed invention.

Therefore, the Appellants again maintain that the Examiner has not provided "technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art" Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inf. 1990). In other words, the Examiner has not pointed to how front loading, where fluid flows through the orifice to the firing chamber, can be considered to be an inherent characteristic of Deeg, where the fluid flows in the opposite direction, from a reservoir into the firing chamber.

Therefore, Deeg does not anticipate the rejected claims because Deeg fails to teach each and every element of the rejected claims, namely, front loading an inkjet head by contacting an orifice with the fluid in a manner so that the fluid flows through the orifice and into a firing chamber.

As discussed above, Deeg does not teach this element, because nowhere does Deeg teach front loading a fluid into an inkjet head by contacting an orifice with the fluid

in a manner so that the fluid flows through the orifice and into a firing chamber.

The Office alleges that "it would have been obvious to a person of ordinary skill in the art to try completely front load of all loading fluids through the orifice to improve the inkjet loading process, as a person with ordinary skill has good reason to pursue the known option within his or her technical grasp" (Examiner's Reply, p. 24)

However, the Appellants respectfully disagree, and note that although the Office alleges that it would have been obvious to "front load" fluids, the Examiner has not provided a single reference that discloses the method of front loading.

Furthermore, the Deeg reference that has been cited as prior art does not suggest the element of front loading, because the inkjet head orifice of Deeg, in its normal and usual operation, is to load analytical liquid into "disposable jet units" (i.e., cartridges) "which contain the analytical liquid (especially reagents or calibrating liquids) in prepacked form" which are then associated with the inkjet head (column 2, lines 22 to 25). Deeg therefore actually teaches away from front loading of fluid, because the method in Deeg is directed to the use of pre-packed, disposable units.

The Appellants maintain that "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti 123 USPQ 349 (CCPA 1959). If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon 221 USPQ 1125 (Fed. Cir. 1984).

The 'prepacked disposable units' as disclosed in Deeg could not be used with the front loading method of the current claims. Furthermore, a front loading method would defeat the stated purpose of using the prepacked disposable units in Deeg. As such, Deeg does not suggest the front loading step of the claimed methods.

Therefore, Deeg fails to make obvious the claims of this Group because Deeg

fails to teach or suggest all the elements of the claimed invention, namely, Deeg fails to teach or suggest front loading an inkjet head by contacting an orifice with the fluid in a manner so that the fluid flows through the orifice and into a firing chamber.

An additional element of Claims 2, 22, 24-28, and 35 is the element of front loading a fluid into an inkjet head by contacting an orifice with the fluid and applying back pressure to the head during the contacting step.

In making the rejection, the Examiner alleges that ""back pressure" is an inherent property of inkjet head for preventing fluid leakages, as evidenced by Cowger et al (U.S. 5,409,134; 4/25/1995)" (Examiner's Reply, p. 23)

However, the Appellants again maintain that not only does Deeg not teach front loading fluid, as discussed above, but Deeg further does not teach the element of back pressure. Nowhere is there disclosed in Deeg the element of "back pressure". Even if, as the Examiner alleges, back pressure is "inherent", as the Examiner has stated, "the fluid or ink in contact with the orifice is suctioned in the head before ejection". (Advisory Action, p. 8) In other words, the cited reference merely discloses suction to prevent leakage. Nowhere in the cited reference or in Deeg is the method of applying back pressure during said contacting step as a method of loading fluid.

Therefore, Deeg does not anticipate the element of applying back pressure because Deeg fails to teach each and every element of the rejected claims, namely, applying back pressure to said head during said contacting step, because Deeg (1) does not teach a front loading contacting step; and (2) does not teach applying back pressure; and furthermore (3) does not teach applying back pressure during said contacting step.

As discussed above, Deeg also does not suggest this element, because a front loading method would not allow for the use of the 'prepacked disposable units' as disclosed in Deeg. "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious.

In re Ratti 123 USPQ 349 (CCPA 1959). If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon 221 USPQ 1125 (Fed. Cir. 1984)." As such, Deeg does not suggest the front loading step of the claimed methods.

Therefore, Deeg fails to make obvious Claims 2, 22, 24-28, and 35 because Deeg fails to teach or suggest all the elements of the claimed invention, namely, Deeg fails to teach or suggest front loading an inkjet head which further comprises applying back pressure to said head during said contacting step.

An additional element of Claims 6 and 23 is the element of washing the head following the actuating step.

In making the rejection, the Examiner alleges that "the instant specification does not specifically define the step of "washing said head", which can broadly and reasonably be interpreted to be any subsequent washing (or cleaning step)." (Examiner's Reply, p. 25)

The Appellants respectfully disagree. For example, washing the head is described in the specification on p. 11, lines 23-29:

> "Where desired, following deposition of the desired amount of protein fluid, the head may be washed and front loaded with another protein containing fluid for subsequent fluid deposition. Washing of the head can be accomplished using any convenient protocol, e.g., via front loading and expelling an appropriate wash buffer, one or more times, by backloading and expelling an appropriate wash buffer, etc. In addition, the head may be manually or automatically wiped clean to remove any sample/wash solution left from the previous deposition."

The Examiner also alleges that "[t]he reference teaches washing steps consisting of metering tap water (reads on washing the head following actuating step as recited in clms 6, 12, 17, 23; See example 4 a)-h) of the reference)" because the washing solution (e.g. tap water) would flow through the ink jet head (thus washing the head)." (Examiner's Reply, p. 25)

The cited reference is shown below:

a) Streptavidin-coated polystyrene tubes (manufactured according to EP-A-0344578) are used. 100 µl of sample or standard are metered into each tube.
b) 10 µl of a conjugate solution which has been filtered on a 0.8 µm filter are applied using a printing head as in Examples 1–3. The conjugate solution contains 18 U/ml of a conjugate consisting of a monoclonal antibody directed against TSH (ECACC 87122202) and peroxidase in 80 mM sodium phosphate buffer (NaPB) pH 7.4.
c) 1 min after delivery of the conjugate, 1 ml of incubation buffer (80 mM NaPB pH 7.4 with 1250 µg/ml of a biotinylated monoclonal antibody directed against TSH (ECACC 87122201), 2 g/l of bovine serum albumin and 1 g/l of bovine IgG) is metered via the metering unit of said system. (The biotinylation of the antibody was carried out in accordance with JACS 100 (1978, 3585–3590) by reaction with N-hydroxysuccinimidobiotin in a ratio of 10:1.)
d) The mixture is then incubated for 60 min.
e) Five washing steps, each consisting of aspiration of the reagent solution and metering of tap water, are carried out with the metering unit of the system used.
f) 1 ml of Enzymun-ABTS ® substrate solution is metered, again via the metering unit.
g) The mixture is incubated for 30 min.
h) The extinction of the substrate solution is measured at 405 nm using the system's photometric measuring device.

The Appellants again point out that the washing steps in step e), "...are carried out with the metering unit of the system..."

Figure 2 of Deeg is reproduced below for convenience:

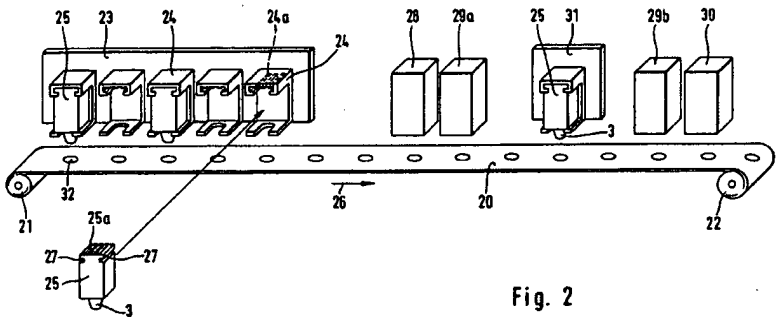

Fig. 2

As shown above, metering unit 28 is a separate element from jet unit 25. The method in Deeg involves applying a solution using "a printing head" (jet unit 25 above), followed by "washing steps", carried out with metering unit 28. In other words, the washing steps are done with metering unit 28, not jet unit 25. There is no disclosure in Deeg of "washing the head following the actuating step" because the 'washing' in Deeg is done with metering unit 28 or wash units 29a and 29b.

It is unclear to the Appellants how "washing steps", carried out with metering unit 28, could possibly flow through or contact the head of jet unit 25, as shown in the above diagram. As disclosed in Deeg, " [t]he analysis procedure is started by applying analytical liquids, especially reagents, to the band 20 through one or more of the jet units 25 of the reagent metering station 23, forming reagent domains 32 on the band." (col. 4, lines 37-40, emphasis added). Then Deeg continues, "[a] sample is delivered through the sample metering unit 28. Where necessary, washing steps can be carried out with the wash units 29a and 29b." (col. 4, lines 47-49). The Examiner also asserts the reference "teaches the ink jet head (element 31) is downstream to the washing unit (element 29a; see Figure 2), which the washing liquid dispensed can "wash" the ink jet head on station 31 when the inkjet head is contacted with substrate" (Examiner's Reply, p. 26) However, the Appellants point out that nowhere in Deeg is this disclosed, nor has the Examiner pointed any reference in Deeg that discloses the element of washing the head. Deeg only discloses that washing steps can be carried out with metering unit 28, or with wash units 29a or 29b. There is no disclosure of "washing said head" as in

the current claims.

Therefore, Deeg does not anticipate the rejected claims 6 and 23 because Deeg fails to teach each and every element of the rejected claims, namely, washing said head following said actuating step.

The Examiner has also rejected claims claims 6 and 23 as being obvious over the Deeg patent. In making this rejection, the Examiner asserts that Deeg teaches or suggests every element of the claims.

As discussed above, Deeg does not teach the element of washing said head following said actuating step. Furthermore, Deeg does not suggest this element, because as above, the washing step in Deeg given by the Examiner is performed with metering unit 28. Additionally, Deeg further discloses: "[w]here necessary, washing steps can be carried out with the wash units 29a and 29b"(col. 4, lines 48-49) thereby actually teaching away from washing the head, because Deeg discloses that washing steps can be carried out with metering unit 28, or with separately provided wash units 29a and 29b. There is therefore no teaching or suggestion in Deeg of "washing said head following said actuating step" as in the current claims.

Furthermore, the Examiner also alleges that "it would have been prima facie obvious for one of ordinary skill in the art to wash the inkjet head after the sample depositing step, because washing steps are needed to clean the inkjet heads after sample delivery so that different samples can be delivered or the inkjet head can be cleaned for further uses". (Examiner's Reply, p. 25)

Again, the Appellants respectfully disagree. First of all, the Appellants point out that the "sample" in Deeg is delivered by "sample metering unit 28", not the ink jet head, as the Examiner alleges (see col. 4, lines 47-48, cited above, and Fig. 2). Secondly, jet unit 25 is used to deliver reagents to band 20 (see col. 4, lines 39-40, cited above, and Fig. 2). Therefore, as the inkjet heads in Deeg do not deliver sample, the Examiner's argument that "washing steps are needed to clean the inkjet heads after sample delivery so that different samples can be delivered" is incorrect.

Furthermore, the Appellants argue that Deeg actually teaches away from washing the heads, because the method in Deeg involves using prepacked cartridges containing analytical liquid. As disclosed in Deeg:

> "A decisive feature of the present invention is that, as regards the reagent delivery, a very simple and flexible adaptation to the requirements of the particular analysis is possible. Thus, by simply changing the jet units 25, the apparatus can be adapted to different analyses, working with different reagents, without having to exchange reagent containers or rinse the feed tubes and metering systems used in conventional systems."

In other words, Deeg discloses that there is no need to "rinse the feed tubes and metering systems" because the jet units 25 are exchanged. There would be no valid apparent reason for one of ordinary skill in the art to wash the inkjet head after the sample depositing step, as the Examiner alleges, because Deeg teaches that the jet units 25 are exchanged, in order to obviate the need for a rinsing step.

Therefore, Deeg fails to make obvious Claims 6 and 23 because Deeg fails to teach or suggest all the elements of the claimed invention, namely, Deeg fails to teach or suggest washing said head following said actuating step.

Additionally, an element of rejected claims 12-21 is front loading a fluid into an inkjet head by contacting an orifice with the fluid and applying back pressure to the head during the contacting step, and washing the head.

As discussed above, the Appellants again maintain that not only does Deeg not teach front loading fluid, but nowhere in the cited references of Cowger or Deeg is the method of applying back pressure as a method of loading fluid during the contacting step. Additionally, as discussed above, there is no disclosure in Deeg of "washing the head" following the actuating step because the 'washing' in Deeg is done with metering unit 28 or wash unit 29a or 29b.

Therefore, Deeg does not anticipate the rejected claims 12-21 because Deeg fails to teach each and every element of the rejected claims, namely, applying back pressure to said head during said contacting step, because Deeg (1) does not teach a front loading contacting step; and (2) does not teach applying back pressure; and

furthermore (3) does not teach applying back pressure during said contacting step. Deeg also fails to teach washing said head following said actuating step. Accordingly, because Deeg fails to teach each and every element of the rejected claims, namely, applying back pressure during said contacting step and washing said head following said actuating step, Deeg fails to anticipate Claims 12-21.

The Examiner has also rejected Claims 12-21 as being obvious over the Deeg patent. In making this rejection, the Examiner asserts that Deeg teaches or suggests every element of the claims.

As discussed above, Deeg does not teach the element of applying back pressure during to the head during the contacting step. Furthermore, Deeg does not suggest this element, because a front loading method would not allow for the use of the 'prepacked disposable units' as disclosed in Deeg. As such, Deeg does not suggest the front loading step of the claimed methods. Additionally, as discussed above, Deeg does not teach the element of washing said head following said actuating step. Deeg also does not suggest this element, because as above, the washing step in Deeg given by the Examiner is performed with metering unit 28 or wash units 29a and 29b" (col. 4, lines 48-49). thereby actually teaching away from washing the head, because Deeg discloses that washing steps can be carried out with metering unit 28, or with separately provided wash units 29a and 29b. Furthermore, Deeg also teaches away from "washing said heads" because because the method in Deeg involves using prepacked cartridges containing analytical liquid. Deeg discloses that there is no need to "rinse the feed tubes and metering systems" because the jet units 25 are exchanged. There would be no valid apparent reason for one of ordinary skill in the art to wash the inkjet head after the sample depositing step, as the Examiner alleges, because Deeg teaches that the jet units 25 are exchanged, in order to obviate the need for a rinsing step.

Therefore, Deeg fails to make obvious Claims 12-21 because Deeg fails to teach or suggest all the elements of the claimed invention, namely, Deeg fails to teach or suggest front loading an inkjet head which further comprises applying back pressure to said head during said contacting step, and Deeg also fails to teach or suggest washing

said head following said actuating step.

Accordingly, in view of the above arguments, the Appellants respectfully request that both the 35 U.S.C. § 102(b) rejection and the 35 U.S.C. § 103(a) rejection of Claims 1, 2, 4-10, 12-28, and 35 over Deeg et al. (U.S.P.N. 5,338,688) be withdrawn.

IV. Claims 1, 2, and 9 are not unpatentable over Claims 19-21 and 23 of Caren et al. (U.S. Patent 6,797,469).

An element of the rejected claims includes a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate in a manner that retains the reagent's functionality.

In making the rejection, the Examiner presented the same argument as the argument over the Caren '469 patent, alleging that the "Appellants have not provided any evidence to indicate that the proteins contained within the quantity of fluid of the '469 patent is structurally different from the "proteins" of the instant claims" (Examiner's Reply, p. 27).

However, again the Appellants respectfully disagree. As discussed above, Caren '469 is directed to deposition of sample, not reagent, on an array. The cited portions of Caren '469 are directed to screening a fluid sample for the presence of an analyte in a sample; specifically a nucleic acid. As described in the specification, "[T]he fluid sample that is deposited on the array according to the subject invention is a fluid sample that is suspected of containing an analyte of interest. In other words, the fluid sample may or may not actually contain the analyte of interest" (col. 4, lines 14-18). It is therefore not a protein reagent as claimed.

Therefore, because Caren '469 does not teach the method of depositing a quantity of fluid containing a protein reagent of interest onto a surface of a substrate, Caren '469 does not make obvious the rejected claims. In view of the arguments above, the Appellants submit that the teachings of Caren '469 fail to meet the requirements for a nonstatutory obviousness-type double-patenting rejection, and

respectfully request reversal of this rejection.

V. Claims 1, 2, and 9 are not unpatentable over Claims 1, 3, 5-7, 9, 10, 12, 17, and 19 of Caren et al. (U.S. Patent 6,221,653).

An element of the rejected claims include a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality.

In making the rejection, the Examiner presented the same argument as the argument over the Caren '653 patent, alleging that reference anticipates the claims (Examiner's Reply, p. 28).

However, again the Appellants respectfully disagree. As discussed in the previous response, Caren '653 is directed to deposition of sample, not reagent, on an array. The Examiner has not pointed to where '653 discloses deposition of a reagent. Nowhere does Caren '653 disclose deposition of a protein reagent onto a substrate; i.e., a substance used in a chemical reaction to detect, measure, examine, or produce other substances, in a manner that maintains said reagent's functionality.

Therefore, because Caren '653 does not teach the method of depositing a quantity of fluid containing a protein reagent of interest onto a surface of a substrate, Caren '653 does not make obvious the rejected claims. In view of the arguments above, the Appellants submit that Caren '653 fails to meet the requirements for a nonstatutory obviousness-type double-patenting rejection, and respectfully request reversal of this rejection.

VI. Claims 1, 2, and 9 are not unpatentable over Claims 1, 5, 9, 11-13, 15, and 18 of Caren et al. (U.S. Patent 6,656,740).

An element of the rejected claims include a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality.

In making this rejection, the Examiner states that the '740 "biopolymer fluid read on a fluid containing a protein reagent because the '740 patent defines the term "biopolymer" to include proteins" (Examiner's Reply, p. 28)

However, the Appellants again assert that the claims of Caren '740 are directed to a method of fabricating an array of biopolymers by in-situ synthesis. In other words, Caren '740 is directed to fabricating, i.e., "building" a feature or "spot" on an array using an in-situ method. Multiple iterative steps are performed in order to form the final 'features' on the array. This is in contrast to the current claims, in which a protein reagent is deposited in a manner that maintains the reagent's functionality. That is, an entire protein reagent is deposited onto the surface of a substrate in a functional form. This is clearly distinguished from a method of building a biopolymer through a multiple step process until a final feature or spot on an array is created.

Additionally, the Examiner states that "the instant specification does not specifically define the term "functionality", which can be broadly and reasonable interpreted to mean any "functions" or activity of the protein." (Examiner's Reply, p. 29)

However, the Appellants respectfully disagree, and maintain that the specification does define "functionality", as cited below:

> "More specifically, if the sum of all of the individual activities of the individual protein molecules in the deposited volume of fluid is viewed as the overall protein activity of the fluid for the deposited volume of fluid, then the deposition process does not substantially change the overall protein activity of the deposited fluid sample, if at all, because the deposition process does not modify a significant percentage of the total number of protein molecules present in the deposited fluid sample. Since a significant percentage of the total number of protein molecules in the quantity of deposited fluid is not modified by deposition according to the subject methods, the total percentage of protein molecules that are modified, e.g., denatured, degraded or otherwise inactivated etc., at least partially or completely, by the deposition process does not exceed about 10%, usually does not exceed about 5% and more usually does not exceed about 1%. For example, where a given quantity of deposited fluid contains 1000 identical antibody molecules, deposition results in degradation or denaturation, either partially or completely, of less than 100 of these molecules, usually less than 50 of these molecules and more usually less than 10 of these molecules, if any. In terms of concentration of the active protein of interest, any change in concentration of the activity or function protein of interest in the sample that occurs in the deposited fluid does not exceed about 20%, usually does not exceed about 10% and more usually does not exceed about 5%." (p. 7, line 8 to p. 8, line 6)

and

> "In terms of the overall protein activity, the amount of modulation, if any, that occurs because of the manner of deposition is typically less than about 10%, usually less than about 5% and more usually less than about 1%. A convenient means of determining the amount of change in overall protein activity caused by deposition is to compare the protein activity of a quantity of fluid that has been expelled or fired from the inkjet to the protein activity of the same quantity of an identical fluid that has not been expelled or fired, e.g., loaded fluid still in the head. The particular assay that is employed to achieve the above comparison necessarily varies depending on the particular nature of the protein and activity/functionality of interest." (p. 8, lines 7-15)

Therefore, the Appellants assert that the meaning of the term "functionality" is clear.

Accordingly, the Appellants contend that the requirements for a nonstatutory obviousness-type double-patenting rejection have not been met, because Caren '740 fails to teach each and every element of the claims, namely, depositing a protein reagent onto a surface of a substrate in a manner that maintains the reagent's functionality. In view of the arguments above, the Appellants submit that the teachings of Caren '740 fail to meet the requirements for a nonstatutory obviousness-type double-patenting rejection, and respectfully request reversal of this rejection.

VII. Claims 1, 2, 6, 7, and 8 are not unpatentable over Claims 1-5, 7, and 11-19 of Caren et al. (U.S. Patent 6,323,043) and Claims 1, 2, 4, and 6 of Caren et al. (U.S. Patent 6,884,580)

An element of the rejected claims includes a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality.

In making this rejection, the Examiner states that the '043 "biopolymer fluid read on a fluid containing a protein reagent because the '043 patent defines the term "biopolymer" to include proteins" (Examiner's Reply, p. 29)

However, the Appellants again assert that the claims of Caren '043 and Caren '580 are directed to a method of fabricating an array of biopolymers by in-situ synthesis.

In other words, Caren '043 and Caren '580 are directed to fabricating, i.e., "building" a feature or "spot" on an array using an in-situ method. Multiple iterative steps are performed in order to form the final features on the array. This is in contrast to the current claims, in which a protein reagent is deposited in a manner that maintains the reagent's functionality. That is, an entire protein reagent is deposited onto the surface of a substrate in a functional form. This is clearly distinguished from a method of building a biopolymer through a multiple step process until a final feature or spot on an array is created.

Accordingly, the Appellants submit that Caren '043 and Caren '580 do not make obvious the rejected claims, because Caren '043 and '580 fail to teach each and every element of the claims, namely, depositing a protein reagent in a manner that maintains the reagent's functionality.

Additionally, an element of rejected Claim 8 includes a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality, wherein the protein of interest is an enzyme. Caren '043 and Caren '580 do not contain the element of depositing an "enzyme", and therefore they do not anticipate the current claims, which contain the element of a depositing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality, wherein said protein of interest is an enzyme.

Accordingly, the Appellants submit that Caren '043 and Caren '580 do not make obvious the rejected claims, because Caren '043 and '580 fail to teach each and every element of the claims, namely, depositing an enzyme reagent in a manner that maintains the reagent's functionality. In view of the arguments above, the Appellants submit that the teachings of Caren '043 and Caren '580 fail to meet the requirements for a nonstatutory obviousness-type double-patenting rejection, and respectfully request reversal of this rejection.

VIII. Claims 1,2, and 4 are not unpatentable over Claims 1, 3, 8, 12, 14, 15, and 18 of Schleifer et al. (U.S. Patent 6,242,266).

An element of the rejected claims includes a method for depositing a quantity of a fluid containing a protein reagent onto the surface of a substrate, in manner that retains the reagent's functionality.

In making the rejection, the Examiner alleges that in the '266 patent "the biopolymer fluid read on a fluid containing a protein reagent because the '266 patent defines the term "biopolymer" to include proteins" (Examiner's Reply, p. 30)

However, the Appellants again assert that the claims of Schleifer '266 are directed to a method of fabricating an array of biopolymers by in-situ synthesis. In other words, Schleifer '266 is directed to fabricating, i.e., "building" a feature or "spot" on an array using an in-situ method. Multiple iterative steps are performed in order to form the final features on the array. This method is in contrast to the current claims, in which a protein reagent is deposited in a manner that maintains the reagent's functionality. That is, an entire protein reagent is deposited onto the surface of a substrate in a functional form. This is clearly distinguished from a method of building a biopolymer through a multiple step process until a final feature or spot on an array is created.

Accordingly, the Appellants contend that the requirements for a nonstatutory obviousness-type double-patenting rejection have not been met, because Schleifer '266 fails to teach each and every element of the claims, namely, depositing a protein reagent in a manner that maintains the reagent's functionality. In view of the arguments above, the Appellants submit that the teachings of Schleifer '266 fail to meet the requirements for a nonstatutory obviousness-type double-patenting rejection, and respectfully request reversal of this rejection.

SUMMARY

The Appellant's prior arguments still stand with equal force for the reasons discussed in the Appeal Brief and for the additional reasons discussed above.

In view of the foregoing discussion, the Appellants request that all remaining rejections be reversed and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

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